REMARKS

Amendments and Added Claims:

Applicants have amended the specification to add the proper reference to the prior application, to add the sequence identifiers to the specification and to correct grammatical or clerical errors in the specification. These amendments do not add any new matter.

Applicants have also amended the claims in a manner that is believed to clarify the claimed invention. Specifically, sequence identifiers have been added to the pending claims, and Claims 59-65 have been added to provide additional dependent embodiments for Claims 32 and 33. Claim 33 has been amended to include the limitations of Claim 32, in anticipation of rejoinder of the method claims with the product claims, as discussed below.

Restriction Requirement:

The Examiner has restricted the claims of the invention into two groups as follows:

Group I (Claim 32), directed to a composition comprising a CDN antibody; and

Group II (Claims 33-38), directed to a method for detecting the presence of CDN in cells.

Applicants provisionally elect, with traverse, the claim of Group I (Claim 32). Applicants submit that the method of Claim 33 (Group II), particularly as amended, requires the use of the antibody of Group I. Therefore, a thorough search for the subject matter of Group I will be sufficient to examine the claims of Group II. In any event, if the elected claims of Group I are found allowable, Applicants reserve their right to amend the claims of Group II, if necessary, to be commensurate in scope with the product claims of Group I, and to request that such amended claims that depend from or otherwise include all the limitations of the allowable product be rejoined and examined for patentability. In re Brouwer, 37 USPQ2d 1663 (Fed. Cir. 1996); In re Ochiai, 37 USPQ2d 1127 (Fed. Cir. 1995).

The Examiner has also required an election of species between Cdn-1 protein and Cdn-2 protein. Applicants provisionally elect, with traverse, to prosecute the species of Cdn-1 proteins. Cdn-1 is encoded by nucleotide sequence SEQ ID NO:6 and is represented by the amino acid sequence SEQ ID NO:7. Claims reading on the elected species are Claims 32-35, 38, 59, 60 and 63. Applicants traverse the species election on the basis that Cdn-1, Cdn-2 and Cdn-3 are related

proteins and that it would not create an undue burden on the Examiner to search for the three sequences or more specifically, for antibodies that bind to the sequences. To require an election between the proteins in this instance only increases the expense to both Applicant and the Patent Office to prosecute antibodies binding to each of the three proteins separately. In any event, Applicants note that such a requirement is primarily, if not solely, intended to facilitate a search by the Examiner. Applicants note that the Examiner is obligated to examine the generic claims and submits that the scope of the claims of the present invention is not limited to the elected species.

In view of the foregoing discussion, Applicants respectfully request that the Examiner withdraw the Restriction Requirement and the species election requirement.

Please direct all future correspondence to the below-named agent and address.

Respectfully submitted,

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Marked-Up Version Showing Amendments

In the Specification:

The title of the application has been replaced with the following title:

--METHODS AND COMPOSITIONS FOR DETECTING CDN APOPTOSIS-MODULATING PROTEINS--

On page 1, the paragraph spanning lines 8-10 has been replaced with the following paragraph:

--This application is a divisional of U.S. Patent Application Serial No. 08/320,157, filed October 7, 1994, now abandoned, which is a continuation-in-part of U.S. Patent Application Serial No. 08/160,067, filed November 30, 1993, now abandoned. The entire disclosure of the prior application is incorporated herein by reference.--

On page 3, the paragraph spanning lines 28-29 has been amended as follows

--Figure 1 depicts the PCR primers used to isolate the cdn-1 probes (SEQ ID NO:1 through SEQ ID NO:5, from top to bottom).--

On page 3, the paragraph spanning lines 32-33 has been amended as follows:

--Figure 3 depicts the nucleotide sequence (SEQ ID NO:6) and the predicted amino acid sequence (SEQ ID NO:7) of cdn-1.--

On page 4, the paragraph spanning lines 4-6 has been amended as follows:

--Figure 5 shows the sequence of the cdn-2 cDNA and flanking sequences (SEQ ID NO:8) and the corresponding predicted amino acid sequence (SEQ ID NO:9) of the cdn-2 protein.--

On page 4, the paragraph spanning lines 7-9 has been amended as follows:

--Figure 6 shows a comparison of N-terminal amino acid sequences of cdn-1 (SEQ ID NO:10), cdn-2 (SEQ ID NO:11) and known bcl-2 family members (SEQ ID NO:12 through SEQ ID NO:19, from bcl-2 through ced-9).--

On page 4, the paragraph spanning lines 10-11 has been amended as follows:

--Figure 7 shows the nucleotide sequence (SEQ ID NO:20) and the predicted amino acid sequence (SEQ ID NO:21) of cdn-3.--

On page 4, the paragraph spanning lines 20-23 has been amended as follows:

--Figure 11 depicts the cdn-1 derivative proteins Δ1, Δ2 and Δ3 (SEQ ID NO:22). The N-terminal residues are indicated by the arrows. The remainder of the derivative proteins is the same as full-length cdn-1.--

The paragraph spanning page 7, line 35 through page 8, line 4, has been amended as follows:

--The invention further embodies a variety of DNA vectors having cloned therein the cdn nucleotide sequences encoding CDN proteins. Suitable vectors include any known in the art including, but not limited to, those for use in bacterial, mammalian, yeast and insect expression systems. Specific vectors are known in the art and need not be described in detail herein.--

On page 12, the following new paragraph has been inserted on line 10 prior to the paragraph currently spanning lines 10-20:

--The invention thus encompasses a method of detecting the presence of a CDN protein in a biological sample comprising the steps of: obtaining a cell sample; lysing or permeabilizing the cells to the antibodies; adding anti-CDN-specific antibodies to the cell sample; maintaining the cell sample under conditions that allow the antibodies to complex with the CDN; and detecting the antibody-CDN complexes formed. The cell sample can be comprised of T cells.--

On page 15, the paragraph spanning lines 6-19 has been amended as follows:

The invention also encompasses therapeutic methods and compositions involving treatment of patients with biological modifiers to increase or [decreast] decrease expression of [cdns] CDNs. Effective concentrations and dosage regimens may be empirically derived. Such derivations are within the skill of those in the art and depend on, for instance, age, weight and gender of the patient and severity of the disease. Alternatively, patients may be directly treated with either native or recombinant CDNs. The CDNs should be substantially pure and free of pyrogens. It is preferred that the recombinant CDNs be produced in a mammalian cell line so as to ensure proper glycosylation. CDNs may also be produced in an insect cell line and will be glycosylated.

On page 21, the paragraph spanning lines 17-23 has been amended as folows:

--The coding region of cdns can also be ligated into expression vectors capable of stably integrating into other cell types including, but not limited to, cardiomyocytes, neural cell lines such as GTI-7, and TNF cell line HT29, so as to provide a variety of assay systems to monitor the regulation of apoptosis by cdn-1.--

In the Claims:

Claims 32-38 have been amended as shown below.

Claims 59-65 have been added.

32. (Once Amended) A composition comprising a monoclonal or polyclonal antibody which [recognizes] specifically binds to a CDN protein selected from the group consisting of: CDN-1 comprising the amino acid sequence of SEQ ID NO:7, CDN-2 comprising the amino acid sequence of SEQ ID NO:9, CDN-3 comprising the amino acid sequence of SEQ ID NO:21 and CDN-1Δ1 comprising the amino acid sequence of SEQ ID NO:22 [but is substantially unreactive with other members of the bcl family].

33. (Once Amended) A method of detecting the presence of a CDN protein in a biological sample comprising the steps of:

a) obtaining a cell sample;

b) lysing or permeabilizing the cells to antibodies;

c) adding [anti-cdns-specific antibodies] the antibody of Claim 32 to the cell sample;

d) maintaining the cell sample under conditions that allow the [antibodies] antibody to complex with [the cdn] a CDN protein; and

e) detecting [the antibody-cdn] antibody-CDN protein complexes formed, thus detecting CDN protein.

34. (Once Amended) The method according to claim 33, wherein the CDN is CDN-1 (SEQ ID NO:7).

35. (Once Amended) The method according to claim 34, wherein the CDN protein is encoded by a nucleotide sequence comprising SEQ ID NO:6 [is depicted in Figure 3].

36. (Once Amended) The method according to claim 33, wherein the CDN is CDN-2 (SEQ ID NO:9).

37. (Once Amended) The method according to claim 36, wherein the CDN protein is encoded by a nucleotide sequence comprising SEQ ID NO:8 [is depicted in Figure 5].

38. (Once Amended) The method according to claim [32] 33, wherein the cell sample comprises T cells.